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Features

Engineering dry particles

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Determining how a particle is formed is an important part of distributing the API. Usually the process involves a wet processing step, but new dry processing methods are gaining favour because of the application possibilities

Used to create new generation materials through the coating of submicron guest particles to large host powders, dry coating is a relatively new technology that can directly attach different sized particles without any solvents or produced waste.Typically, wet methods have been employed, through mechanical means such as pan coaters or through deposition or interfacial polymerisation. This has been done predominantly to form barrier or protective layers, giving release control, atmospheric protection or taste masking in the case of pharmaceutical applications. However, resultant waste streams, often with VOCs, cause added expense and inevitable environmental concerns. Dry coating can be used to engineer a more extensive variety of composite materials with a wide range of applications.

The application of mechanical force to a mixture of fine and coarse particles will form an ordered mixture where guest particles are sufficiently small as to be held to the surface by Van-der-Waals forces.

Further mechanical action can cause these particles to generate a continuous coating in the form of a non-porous film or porous layer, **figure 1.**

angle of repose

Significant changes in the properties of the original particles can be observed, including electrical conductivity, flowability, solubility, wetability and shape.

Pioneered by Hosokawa Micron in Japan through the development of its Angmill, the Mechanofusion system generates surface fusion through a combination of high shear and compression forces acting on the particles. This system is now being used in a number of industries, including inhaled medicines.

An example of the effects achievable with dry coating in the Hosokawa Mechanofusion system is PMMA particles in the size range 5-15mm coated with TiO_2 (15-50nm). These show a change in flow properties when Mechanofused, which is indicated by the angle of repose as measured using a micron powder tester. It should be noted that the angle of repose shows a strong relation to shell thickness. Below 13nm shell

EXHIBIT 3

thickness of TiO_2 the angle is seen to increase.

Increasing the layer thickness beyond this causes the angle of repose to fall. It can be shown that once the thickness of the shell coating is greater than the particle diameter of the TiO2 this increase in flowability occurs indicating that simple mixing or even loose coating cannot give this effect, **figure 2**.

Coatings can be classified in a number of ways: embedding, encapsulation, filming, surface covering and loose coating. It is also possible to perform a number of coating operations and produce distinct layers on a particle or modify particle shape.

The nature of coating and whether or not a dry coating is achievable through mechanical action is relatively hard to predict and has generally been determined empirically. Modelling has not yet been effectively carried out on the macro or micro scale, however the forces acting on the particles can be seen as being proportional to the angular speed of the Mechanofusion bowl. Furthermore, this force increases as the distance between the compression head and side wall decreases, **figure 3**.

Additional considerations of the powder properties can determine the nature of coating formed. The ratio of host and guest particle size, fracture toughness and ductility along with melting points will all have an influence on the ability to form a dry coating and should be identified at an early stage.

A simple relationship between melting point and guest particle size indicating suitability for fusion is given in **figure 4** and has been determined from a number of trials.

active application

The principle of operation is shown in **figure 3** where a quantity of each of the powders is measured into the chamber. The bowl rotates forcing powder to circulate and be compressed between the stationary compression head and the sidewall.

The intense forces mentioned earlier can cause sufficient local heat to fuse materials together with very strong physical and chemical bonds.

A scraper is used to increase circulation of the materials and thus ensure that all host particles can be coated. The jacketed wall can be cooled and this prevents the bulk material, which is in continuous circulation, from overheating.

A number of application areas for the Mechanofusion are shown in **table 1**. For active pharmaceutical ingredients (APIs), the process involves a coating of an organic carrier material with active ingredients, with the objective of achieving a homogeneous distribution of the active ingredients, improved delivery, and dissolving power.

Whether aiming to improve the flow properties of powders applications, changing the particle shape or embedding active pharmaceutical powders into carrier materials, dry powder coating and the Mechanofusion system is opening up a new generation of possibilities for composite materials.

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